Neymann and Osborne. While finding their methods effective, we occasionally have resorted to other means of inducing fever. We employed several ways; namely, the conductive, the convective and the conversive methods. One method was an incandescent-light cabinet, the degree of heat being controlled by socket switches. We found that maintaining febrile temperatures of 105 degrees F. for several hours produced symptoms of heat stroke. We therefore soon discontinued the use of cellotex cabinets. Lately, Atsatt and Patterson of the Santa Barbara Cottage Hospital, as well as Bishop, Warren and Lehman, have advocated the incandescent-light method in preference to all others.

The induction of high fever by electromagnetic fields having been developed, we soon followed the lead of others in using a large canvas bag of the zipper type, thus enclosing the patient to prevent heat loss. The use of induced short waves and by means of the cable, pancake-coil, and Kimball Cabinet, afforded us the simplest and safest way of any method used. The pathologic reactions of fever, such as abdominal cramps, nausea, vomiting, tetany, headache, and vasomotor collapse do not occur when this method is used within the range of fever adopted.

Lately there is a tendency to permit the production of artificial fever in homes and in physicians' offices. It is not my purpose to determine the method and the place where artificial fever be induced, but we should realize that, at best, the patient is infrequently brought to the border-line of disaster. It is therefore evident to me that when temperatures of 105 to 106.7 degrees F. are maintained for several hours, there must be constant medical and technical supervision.

Asthmatic cases in our hands have received little benefit from fever therapy.

Regarding the questions propounded by Drs. Phillips and Coulter relative to high environmental temperatures in air-conditioned cabinets producing sterility in the male, we are unable to give any information; but our experiments with animals proved that sterility is produced when the incandescent light cabinet is used. We have set a definite time for the culmination of our observation. Then we will make a final report as to the refunctioning of the generative organs.

Printed in U. S. A.

PRESENT STATUS AND TECHNIC OF ARTIFICIAL FEVER *

UPTON GILES, M.D.

NEW ORLEANS

For the past fifty years physicians[45-50] have suspected that fever might be part of the defensive mechanism of the body against invading microorganisms. It was Wagner-Jauregg,[49] who first successfully produced fever in hopeless paretics by malarial injections, which demonstrated the soundness of the concept. Previous to this time, in the treatment of syphilis, gout, arthritis and other chronic conditions, increased bodily heat was induced mostly by physical measures. These were applications of hot blankets, hot air, hot water, steam and mud from natural or artificial sources. While these measures were used empirically, distinct beneficial results were obtained.

In 1884, Phillips,[52] while visiting Hot Springs, Arkansas, experimented on himself and demonstrated the value of temperature-rising baths. Since Jauregg's epochal experiments, many other methods of producing therapeutic fever have been evolved and used with varying degrees of efficiency and safety.

Of the medical or non-physical methods, the injections of crystalloid and colloid substances[41] and of heteroproteins, such as peptones, milk[54] and casein, may be mentioned. Others have injected vaccines prepared from typhoid, paratyphoid and other microorganisms.[20] Inoculations or organisms from erysipelas, undulant fever,[35] rat bite fever[38] and tertian malaria[12-49] have been employed. These methods, usually classified as physiologic, really should be grouped as pathologic, for they depend upon the reaction of the body to the introduction of a foreign substance. The reaction in different individuals varies, and can neither be predicted nor entirely controlled in all instances.

Effect of Malaria Treatment

Following v. Jauregg's and Kyrle's[23] astounding results in paresis with malarial plasmodia, this form of therapy became widely used both in Europe and America. Although malaria has been our most satisfactory method of treatment in paresis, it has many dangers. In 100 cases reported by Bahr[3] and Breutsch,[4] 23 died during or following the malarial paroxysms. In a recent review of the literature Karnosh and Williams,[26] collated 580 cases of paretics who had received inoculations of malaria. These showed a wide array of symptoms and complications with a death rate of 12.7 per cent. Hemorrhages, hematomas, and non-inflammatory ulcers were considered specific lesions due to malarial infections. Enlargement of the spleen and rupture of this organ in some cases produced shock and immediate death. In addition, after injection of the malarial organism, many rapidly fulminating septic states developed, thus suggesting a symbiotic relationship between the plasmodium and many pathogenic organisms. Evidence of serious complications were noted and include jaundice; cyanosis of varying degrees; paroxysm with a temperature of 105.8 degrees F. lasting eight hours following the chill; blood urea of 60 mg. per 100 cc.; and low temperature accompanying an unusually high pulse and respiratory rate. Regarding re-

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* From the Department of Physical Therapy, Charity Hospital, New Orleans.

* Read at the meeting of the Southern Section, American Congress of Physical Therapy, New Orleans, March 23, 1936.

sistance, physical habitus was no index, for the robust appearing individual developed severe collapse as often as the asthenic patient. Bronchopneumonia was found in thirty-five per cent of the fatal cases. It is of significance to state that in some instances, we are giving a disease that is difficult to cure; some individuals, particularly the colored race, exhibit an immunity to malaria. We know of no way of controlling the intensity and severity of the malarial attacks without stopping them completely.

There is a vast difference of opinion regarding the action of the various forms of hyperpyrexia. Schamberg and Rule[39] showed that repeated hot water baths not only prevented the appearance of characteristic lesions of experimental syphilis in rabbits inoculated with spirochaeta pallida, but caused testicular syphilomas and secondary syphilitic ulcers to disappear. Some think there is a specific biologic interreaction of some sort between spirochaeta pallida and plasmodium vivax. Breutsch and Bahr[4-3] believe that clinical remissions in paresis result from a response of the reticulo-endothelial system to the malarial organism. In this, the height of the temperature bears little or no relation to the question of recovery. Neither of these theories has been confirmed. Some are of the opinion that the benefit derived is due to the fever itself and not to the chemical changes in the body resulting from the introduction of any particular foreign organism. Others believe the therapeutic effect in syphilis is not due to fever alone, but possibly to a combination of the fever and its accompanying biologic reaction. To support this view, O'Leary[34-43] states that he has observed patients who had undergone "malarial therapy for active neurosyphilis which appeared during the stage of acute syphilis, developed cutaneous and mucous membrane recurrences six months or more after the fever treatment; likewise, the appearance of cutaneous gumma in paretic patients following fever therapy is evidence that the spirochetes were not destroyed by the heat." To further confirm this view, it is significant that the good results from fever therapy required a year or more to develop.

Long after the discovery by d'Arsonval that high frequency current raises the bodily temperature, came another confirmation by Binger and Christie[2] that heat could be produced in living tissues. D'Arsonval's discovery stimulated Neymann[31] to treat his patients by means of artificial fever by induced high frequency current. He thought fever induced in this manner should settle the problem of the spirocheta pallida and plasmodium vivax with reference to specificity or the biologic interreaction theory. The published results of Neymann and Osborne,[31-32] and King and Cocke,[22] pioneers in this form of therapy, demonstrated that therapeutic results obtained by diathermy equaled those of malarial therapy without the fatalities usually occurring by the latter method. Fatalities following the injection of malaria in some series of cases were as high as 23 per cent, with a general average of 12.7 per cent, as compared to one per cent or less in induced fever therapy by physical measures.

Through the demonstration of the value of this type of therapy by physical measures, many mechanical means were produced to induce therapeutic fever. They are listed as follows, but not necessarily in order of their evolution.

1. Hot Water Baths (used for many years empirically).
2. Diathermy.
    (1) Conventional or damped type of high frequency current.
    (2) Short wave or undamped type of high frequency current.
        a. Electrostatic field.
        b. Electromagnetic field.

3. Electric Blankets.
4. Cabinets.
    A. Heated Air Cabinets.
        (1) Humidified air blown over patient.
            a. Air heated by resistance units.
            b. Air heated by resistance units and incandescent bulbs.
        (2) Still air cabinets.
            a. Heated by incandescent bulbs.
    B. Condenser field cabinets.
        (1) Patient heated only by electrostatic field.
        (2) Patient heated by electrostatic field in conjunction with heated air.
            a. Hot air heated by incandescent bulb.
            b. Hot air heated by resistance unit.
    C. Inductotherm cabinets.
        (1) Patient heated entirely by electromagnetic induction.
        (Air is humidified in cabinet only for comfort and insulation.)

The therapeutic value of artificially produced fever is fairly well established. Artificial fever is known by various writers as hyperpyrexia, hyperthermia, pyrexitherapy, pyretotherapy, thermogenesis, electropyrexia, radiothermy, inductothermy, inductopyrexia and aseptic controlled fever.

It is not the purpose of this paper to attempt to determine the best method to use, for the one which is advantageous to the patient, producing the required fever with the greatest amount of comfort and safety should be employed. We also wish to outline the technic of fever therapy and to state why electromagnetic induction is a valuable method of treatment in many cases.

Electromagnetic Field

Raising the body temperature by means of induced heat is both unique and logical. Heat is produced by electromagnetic induction from within the patient's body by means of an alternating electromagnetic field. The patient is placed within this field; eddy currents are set up in the vascular tissue, thus causing a gentle rise in temperature. Without any contact of electrodes the alternating field is induced in the patient's body by means of a coil. Thus the heat is produced within the patient's body and is not conducted into it by a higher environmental temperature.

Many of the undesirable physiologic effects are avoided. Because of the fact that no excessively high temperature surrounds the patient, no danger of burns from this source exists. As the electromagnetic field is not distorted by moisture spots appearing on the patient, no danger of burns exists from the concentration of heat within any small area. This method does not disturb the basic physiologic relationship, and therefore seems to approach the ideal in both comfort and safety. The reverse, however, is true whenever external heat is applied to any extent.

This method can be used in any one of several ways for producing artificial fever. The patient may be placed in a fever bag made of suitable heat-insulating material. This bag is equipped with a "zipper" arrangement which closes the bag tightly, encircling the patient, only his head protruding. The alternating field is created in either of two ways when using the bag. The coil can be placed around the outside of the bag (fig. 1) encircling

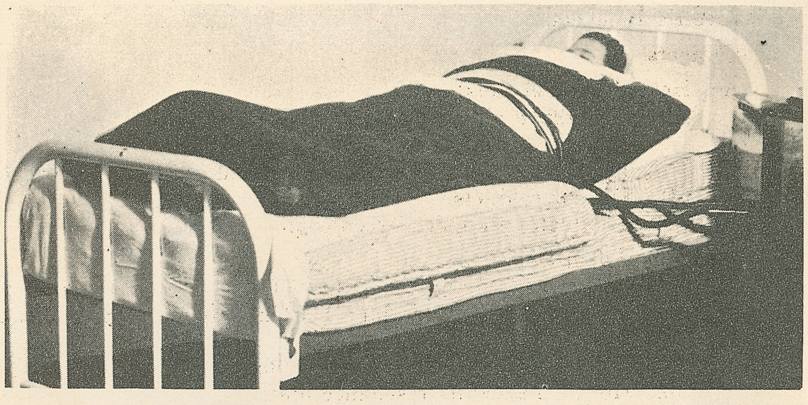

Fig. 1 — Illustrating the technic of Electropyrexia. Three turns of the closely wound cable is placed around the outside of the treatment bag encircling the patient. The third turn of the long cable is omitted here for purpose of photography.

the patient, or it may be used in "pancake" form (fig. 2); in the latter case a disc twelve inches in diameter, which contains the coil, is placed near the patient. In both cases the electromagnetic field is thus induced in the patient's body without any contact whatsoever.

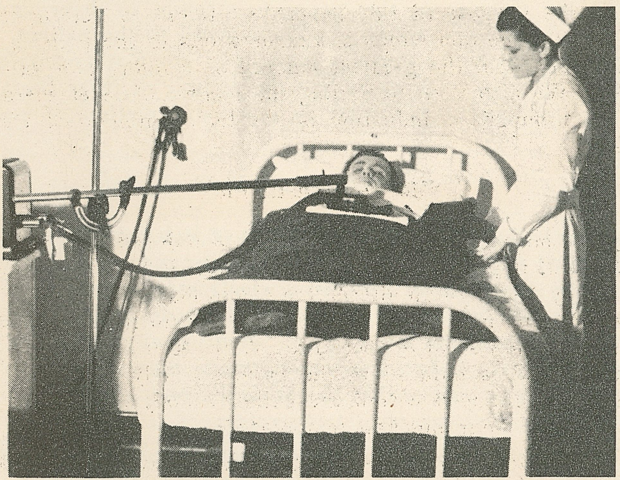

Fig. 2. — Illustrating the use of the Pancake Coil which permits freer movement of patient.

The Kimble cabinet (fig. 3) is another method for the production of artificial fever. This apparatus consists of an air-conditioned cabinet in which the patient lies with his head protruding through an opening. The patient is surrounded by an atmosphere of conditioned air which is just comfortably warm. This SLIGHTLY warm air is not for the purpose of heating the patient, but, by maintaining approximately the same temperature in the cabinet atmosphere as within the body, heat dissipation is prevented, insulating properties are greatly augmented, and the patient is made increasingly comfortable. Heat is applied to the patient by means of a "pancake" coil, (fig. 4) placed on an adjustable bracket inside the cabinet and directly over the patient. The ends of the coil protrude through holes provided for them and are plugged into and energized by the apparatus. The slightly warm air is passed over a humidifier, which adds further to the comfort of the patient. The temperature of the air inside the cabinet is automatically maintained at 100 degrees F. by a thermostat. Rectal temperatures are obtained through a special door. Thus all the good points of the cabinet method are incorporated and most of the undesirable effects avoided. The current consumption when using the Kimble cabinet in conjunction with the inductotherm is much smaller than with the hot-air cabinet. This is due to the excessive current consumption as used in the grid type resistance units which some-

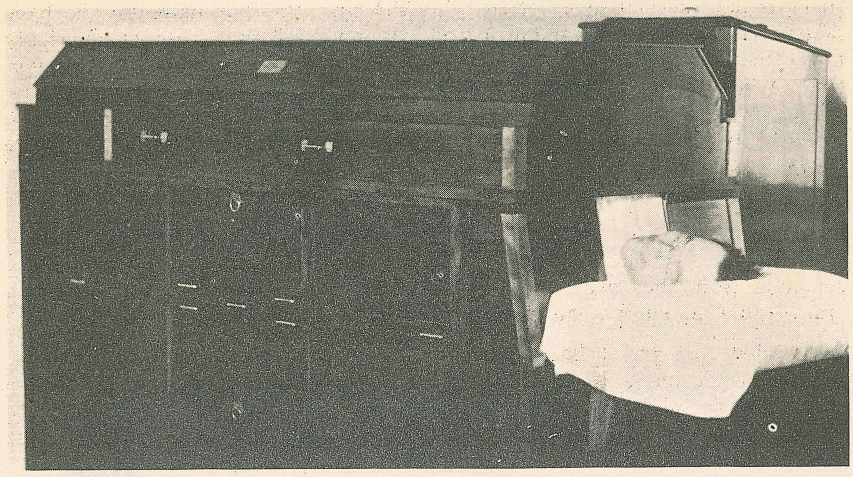

Fig. 3. — Illustrating the Kimble Cabinet. Heat is induced from a coil of the Pancake type. The coil is energized by means of the Inductotherm.

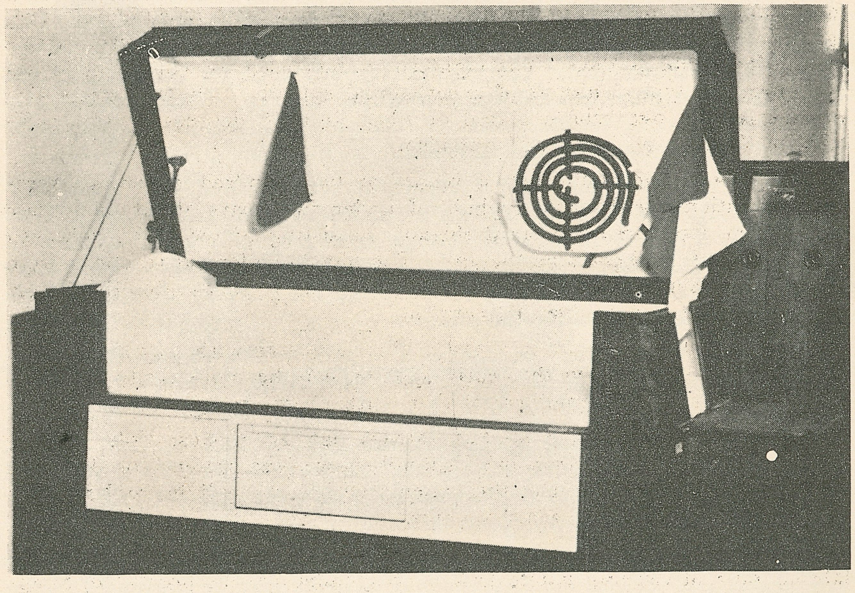

Fig. 4. — Illustrating the Pancake Coil of the Kimble Cabinet. The coil is raised or lowered by means of an adjustable bracket inside the cabinet and placed directly over the patient.

times require special lines for carrying the current. The patients who have taken treatments both in the insulated bag and the Kimble cabinet invariably favor the latter. We have observed that the pulse of patients is slightly more rapid when taking treatment in the cabinet than when taken in the bag, but too few comparative tests have been made to state this as a fact. The patient's temperature has ranged between 105 and 106 degrees F. for five hours. Temperatures of 107 degrees F. have not as yet been induced.

Clinical Results

Syphilis. — From a sufficiently large number of experiments we may safely conclude from the result obtained, that high body temperature exerts an unfavorable influence upon the causative organism.

Weichbrodt and Jahnel[55] placed rabbits with scrotal chancres in an incubator producing a temperature range of 104 to 107.6 degrees F. These animals were subjected to this temperature 30 minutes once or twice daily for three to five weeks. After the second day the spirochetes gradually lost their motility, became less in number, and finally disappeared.

Carpenter, Boak and Warren,[13] by means of the diathermy current, prevented the development of chancres in twenty-one out of twenty-five rabbits in whom treatment was begun five and seven days after inoculation. Two rabbits developed lesions but became normal after further diathermy treatment. Two rabbits died. The eighteen rabbits used for control purposes developed the typical lesions of experimental syphilis. These workers also discovered that one febrile period of 106.7 to 107.6 degrees F. was sufficient to destroy the inoculated organism.

In 1924, Kyrle[23] published a report of two hundred thirty-two seropositive patients with early syphilis of under two years duration. They were given a course of malarial therapy consisting of ten chills, followed by a course of arsphenamine therapy. The blood serological reactions were favorably influenced in two hundred thirty of the patients after this single pyretochemotherapy course of treatment.

Richet and Dublineau[37] in a series of experiments with animals and human beings demonstrated that early syphilis may be more easily cured by combined fever and chemotherapy than with chemotherapy alone.

The combined clinical studies carried out by Stokes, Cole, Moore, O'Leary, Wile, Clark, Parron and Usilton[44] showed the presence of abnormal spinal fluids in 33 per cent of the patients with early syphilis, and 56.1 per cent of patients with secondary syphilis.

With the information noted above and with the hope that the disastrous late neural and visceral manifestations of syphilis may be prevented, Simpson initiated his régime of sustaining a fever temperature above 105 degrees F. with the Kettering apparatus for fifty hours and thirty injections of antisyphilitic chemotherapy. He subjected twenty-six patients, none of whom had previously received treatment, to this method of treatment. As a control measure six patients with primary or early secondary syphilis were treated with only fifty hours of fever therapy above 105 degrees F. A second control group of fourteen patients with primary and early syphilis received only thirty weekly chemotherapeutic injections. His experiments gave suggestive evidence that fever therapy alone or chemotherapy alone is often inadequate. It also demonstrated that combined fever and chemotherapy is a superior form of treatment in early syphilis, particularly in patients who do not respond to orthodox therapy.

Dementia Paralytica. — Working with the Kettering apparatus, Simpson[43] reports twenty cases of dementia paralytica, each completing a course of fifty hours of fever therapy in addition to thirty conventional injections. Of these, twelve showed complete clinical remission and two have been restored to a working status; thus fourteen patients, or 70 per cent, have been socially rehabilitated. Four patients were accorded 50 per cent clinical improvement while only two were regarded as receiving 25 per cent improvement. No relapses have occurred since treatment.

Tabes Dorsalis. — Simpson reported results in ten patients afflicted with tabes dorsalis who had received chemotherapy. Three of these had received malaria therapy, one of whom had temporary remission after the first inoculation. Ataxia was present in nine; lancinating pains and gastric crises were present in all. Two patients with ataxia were restored to a normal gait; six showed improvement; while two showed no change. Usually after the second or third treatment, lancinating pains in each case disappeared. Normal function was restored in one case of so-called cord bladder.

Tabetic Form of Dementia Paralytica. — Out of seven patients treated by Simpson, six showed improvement in mental orientation; root pains in each disappeared; one patient with cord bladder was restored; one patient restored to normal gait; four were improved in gait.

Diffuse Central Nervous System Syphilis. — In this group Simpson reported thirteen patients with varied manifestations of neurosyphilis which could not be definitely classified as dementia paralytica, tabes dorsalis or the tabetic form of dementia paralytica. Six were congenital and seven were acquired. In this group ocular symptoms predominated. Symptomatic remission occurred in nine of the thirteen patients; moderate improvement, in three; and in one, no improvement at all.

Asymptomatic Neurosyphilis. — In seven patients with asymptomatic neurosyphilis, spinal fluid reactions were reversed to negative in six and less positive in one. All patients had had no effective chemotherapy.

Resistant Seropositive Syphilis. — All of these patients are classed as so-called Wassermann-fast cases. Simpson states that intensive courses in chemotherapy had been administered to all. The serological reactions were reduced to negative in four, became less positive in two, and remained positive in one. Spinal fluid reactions remained negative in all.

Treatment of Neurosyphilis at the Charity Hospital

While Simpson in his classification of cases endeavored to establish a régime of pyretochemotherapy, our investigation has been more clinical. We feel that sufficient evidence has already been given by Neymann, Simpson and others to justify the acceptance of pyrexia as a treatment of syphilis of the central nervous system. Our efforts have been directed toward the relief of otherwise hopeless cases; namely, dementia paralytica, tabes dorsalis, taboparesis and resistant seropositive syphilis (Wassermann-fast cases) which, in our group was usually accompanied by cardiovascular, optic atrophy and other complications.

Twenty-two cases were selected for treatment with fever therapy. These were growing progressively worse under exclusive treatment with tryparsamide and other forms of heavy metal. Three had received inoculations of tertian malaria with no benefit. Several patients were not physically fit subjects for malaria therapy. Of this group six showed improvement, eleven marked improvement; and five, spectacular improvement.

We have used electromagnetic induction only as a last resort in those cases of neurosyphilis who could tolerate no other forms of therapy enumerated above, or who were growing progressively worse under a conventional régime. We realize that this is not a fair evaluation of pyretotherapy, for we have selected seemingly hopeless cases. It has naturally been the heroic method as a last resort. The general comment elicited from this group was that within two or three days after each fever session, they felt much better, and after each successive treatment, most patients expressed a feeling of well-being.

For comparative purposes, 21 cases of neurosyphilis were inoculated with tertian malaria with the following results: Ten showed improvement; four marked improvement; and two evidenced spectacular improvement. Of the five malarial cases that showed no improvement, three were later treated by electromagnetic induction, with improvement of subjective and objective symptoms, as reported by Dr. Howles.

The literature shows marked variations in remission in neurosyphilis from fever produced by malaria and mechanical measures. Indiscriminate selection of patients accounts for the diversified results obtained even though identical methods of treatment have been employed. As for example Neymann[5] reported ten mild cases of dementia paralytica who had eight remissions of symptoms following fever therapy. Later Neymann and Koenig reported that fifty demented cases had only twelve remissions.

This means of selection of cases illustrates the almost contradictory reports appearing in the literature.

Gonococcic Infection. — Carpenter, Boak, Mucci and Warren[12] undertook to ascertain the thermal death rate of gonococci. This they did by consecutively subjecting fifteen strains of gonococcus to temperatures of 104, 105.4, 106.5 and 107.3 degrees F. All the strains subjected to these temperatures had been cultivated for a period varying from one month to twelve years. The oldest culture best tolerated heat. Notwithstanding this variation in tolerance, 99 per cent of the cultures could not withstand a temperature of 105.4 degrees F. for more than four or five hours. One per cent required 23 hours for destruction. At a temperature of 106.5 or 107.3 degrees F., 99 per cent were destroyed in two hours. One per cent required heat of 106.5 degrees F. for from seven to twenty hours. To the thorough investigation of Carpenter, Boak, Mucci and Warren we owe the possibility of rapidly curing gonococcic infection. No other microorganism has been subjected to a temperature tolerable by the human to cause its destruction.

The most spectacular success has undoubtedly been obtained in gonorrheal infections, including complications of prostatitis, salpingitis, periurethritis, and cervicitis. Desjardins and his co-workers[15] state that in 90 per cent of the gonorrheal cases three to six sessions of sustained fever of 106 and 106.7 degrees F. of five to eight hours duration are sufficient for a complete and permanent cure.

Arthritis. — In gonococcal arthritis the results of fever therapy have been astounding. The work of Short and Bauer,[46] Hench, Slocum and Popp[17] and Slaughter and Trautman shows that in gonococcal arthritis fever therapy has a sterilizing effect, while in the non-specific, infectious type, the causative germ may not be susceptible to heat. In a survey of rheumatoid patients,[46] treated by diathermy 20 per cent were improved, 28 per cent remained unimproved, and 52 per cent were rendered definitely worse. With gonococcal arthritis there is a striking contrast, 66 to 90 per cent having been reported as "cured," and none without some benefit from the treatment. It is therefore important to point out that patients with chronic, infectious arthritis have only one chance in five for recovery. With them, hyperthermy should not be used to the exclusion of other methods. In gonococcal arthritis one hundred per cent recovery may be expected.

Other Diseases. — Favorable reports appear in the literature on the treatment of the following diseases by artificially induced fever: Intractable bronchial asthma, chorea, corneal ulcer, pulmonary tuberculosis (mild), epidemic encephalitis, bronchitis, cystitis, pyelitis, osteomyelitis, multiple sclerosis, chronic sinusitis and paralysis agitans. The treatment of diseases other than neurosyphilis, gonococcic infection and its complications is still in the experimental stage.

Contraindications. — Contraindications to the use of fever therapy will vary with the degree of temperature elevation.[8] A few degrees of fever certainly will not place as much of a burden on the cardiovascular and other systems as would a higher elevation in temperature.

Advanced age is usually considered a contraindication for fever therapy; however, ages from two to seventy-five are reported in the literature. Patients with advanced pulmonary tuberculosis, renal or cardiac disease should not be subjected to fever therapy. Any contraindication to major surgery is likely to be also a contraindicated to fever therapy.

Technic

The following régime is used in our production of fever. The patient is first subjected to a physical, neurological and laboratory examination. He is given an enema the night before treatment or at about five in the morning of the treatment. Breakfast is limited to fluids. Three grains of sodium amytal or some other sedative is given as the patient leaves the ward. On arriving at the physical therapy department at seven-thirty, the patient is weighed and placed on the fever bed. A terry-cloth or large bath towel (fig. 5) is wrapped around the patient. He is then placed in an insulated zipper bag (fig. 1) the head only remaining exposed. The mattress on the fever bed is in two parts (fig. 5). Between them is an opening into which the heating coil is introduced. This coil is wrapped three times about the body of the patient (fig. 1). The full force of the apparatus is employed until the temperature of the patient registers 104.5 degrees F. The current is cut off to permit the usual coasting upward of one-half degree of temperature. The temperature, pulse, and respiration are taken and recorded every fifteen minutes.

Many patients will retain a temperature of 105 degrees F. for several hours after an interruption of the current; others will require earlier reestablishment of connection with heat. The temperature of 105 degrees F. is usually reached in sixty or ninety minutes and maintained for five hours. Usually, at about noon, the patient becomes restless and requires another sedative. Fluids, such as 0.6 per cent saline and water, are given sparingly until a temperature of 105 degrees is reached. Then fluids may be administered more often, if desired, 1500 to 2500 cc. being the usual amount given.

The patient is moved from the fever bed; then he is placed on a dry bed and covered with one or two blankets. At this time the intake of fluids is forced. The temperature rapidly descends from 105 to 103 degrees F. from which point it proceeds more slowly to normal. It requires from forty-five minutes to an hour for the temperature to reach 100 degrees, when a bath is given. The patient is sent to the ward where an infusion of ten per cent glucose in normal saline is administered. In two hours the patient is usually up about the ward and is feeling fine. When treatment is given in the bag, the patients lose an average of six pounds; while treatment given in the

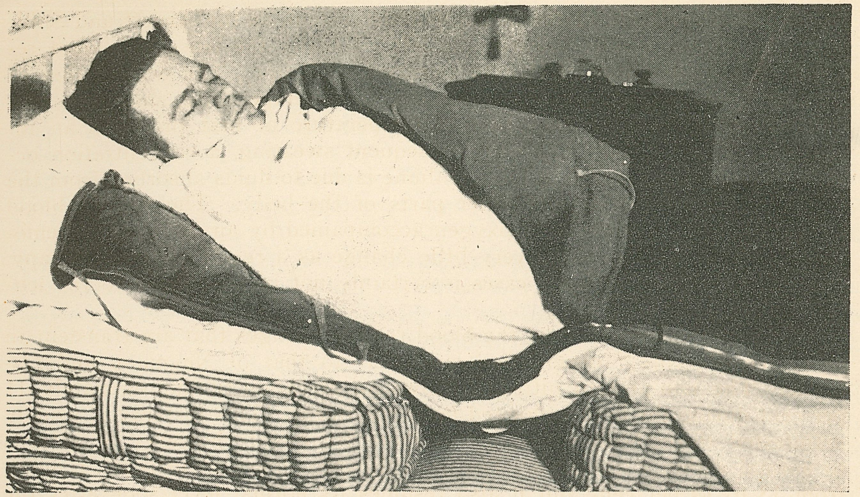

Fig. 5. — Illustrating the proper arrangement of terry cloth about patient's neck to prevent heat loss. Note the trough or separation of the upper mattress. This separation permits an air space between the coil and patient which eliminates skin burns.

cabinet causes a loss of from one to two pounds. Treatments are given biweekly.

Physiologic Manifestations

In the production and maintenance of fever in the body, it is inevitable that profound biochemical and biophysical changes occur.[8] With a rise in temperature there occurs an increase in pulse rate; its rapidity is found to be generally proportionate to the temperature elevation. The increase is approximately 6 to 10 beats per minute for each rise of one degree F. The velocity of the blood flow is accelerated.

The effects of a temperature rise invariably cause an early elevation of blood pressure which apparently is of short duration. This is followed by a gradual decrease of blood pressure to a point below the reading normal for the patient. Invariably there is an associated lowering of the diastolic pressure, usually from 10 to 35 mm. of mercury. When employing the usual auscultatory method of taking blood pressure, the mercury in the manometer infrequently descends to the zero mark. This phenomenon is believed to be due to a wide open aortic ring, but the result of an increased heart rate and dilatation of the peripheral vessels.

The blood picture shows most interesting changes. Slaughter and Trautman state that there is a fluctuation of the white cells from 10,000 to 50,000 throughout treatment. The percentage of neutrophilic polymorphonuclear leucocytes is increased and that of the lymphocytes correspondingly decreased. "The neutrophilic polymorphonuclear leucocytes constitute the most of the early response. Lymphocytes early in the treatment drop to a low count and may be as low as 200 to 500 cells. Only rarely do they show tendency to reappear during the treatment. This reappearance of lymphocytes is usually for a short time only. There is a reappearance of lymphocytes to normal a few hours after treatment." During the first phase of the treatment, just before the initial rise, there may be a temporary decrease in number of white blood cells. This temporary decrease is considered to be an expression of blood dilution. The increase of the white cells is probably due to the stimulation of the hematopoietic system, as the Arnett and Shilling index shows a shift towards the left. Usually the leucocyte count returns to normal within twelve to twenty-four hours. The acceleration of the leucocytes is in proportion to the degree of temperature, similar to that of a chemical reaction. Elevation of temperature at first produces an increase of blood volume, but with subsequent sweating, a concentration occurs. The initial increase in blood volume is due to fluids absorbed from the intestinal tract, muscles and other parts of the body. The venous blood contains greater quantities of oxygen accompanied by an increase of hemoglobin. The red cells show very little change as a result of fever therapy. The slight increase in some cases is certainly not in proportion to the leukocytic increase.

Chemical examination of the blood reveals changes that are transient in character. Perkins',[53] observation is similar to that of Neymann and Osborne. The non-protein nitrogen shows an elevation of approximately 11 per cent during the first prolonged fever treatment. This increase is usually manifested throughout the series of fever treatment; however, it returns to normal within a few days. The urea nitrogen shows an increase, ranging from 13 to 19 per cent, but it also resumes its normal level soon after the elimination of the fever. The blood sugar changes show an increase of approximately 20 per cent. No appreciable increase is observed in the uric acid and creatinin contents of the blood. The blood shows a temporary decrease in chlorides, if there is a failure to administer saline during the treatment. The literature seems to contain conflicting data regarding the effect of increased temperature on the blood-immune bodies. The gastric secretion shows a reduction both in free and total acids as a result of temperature elevation.

The brunt of early rise of temperature is borne by the cutaneous surfaces. The temperature of the skin varies considerably in different parts of the body. Temperature variations affect the skin by producing changes in its vascular mechanism, such as sweating and evaporation of fluids. There is a loss of CO_2 during an excessive and prolonged temperature rise, accompanied by increased respiration and alkalosis. The hydrogen ion concentration shifts toward the alkaline side with increased plasma pH values.

Elevations of temperature of the body tissues produce an increased metabolism. According to the law, van't Hoff,[14] a rise of 10 degree centigrade increases the rate of oxidation two and one-half times.

The rationale of fever is not thoroughly understood. Induced fever by artificial measures is different from that produced by infectious processes. By means of the high frequency current, electrical energy is converted into heat within the body. The heat generated is the result of resistance offered to the current by the body tissues. Fever is produced by convective and conductive measures, such as radiant energy, when it is applied to the skin over a large area. By means of the capillary bed of the skin, there is an absorption of the radiant energy and the warm blood is carried to other portions of the body. Fever as a result of pathologic conditions is produced from sources entirely within the body, and is devoid of heat elimination.

Reaction in Fever Therapy. — There are several types of reactions which may occur as a result of fever treatment, but their occurrence has been decreased considerably by gained knowledge and experience. Restlessness is not uncommon, but can be controlled by sodium amytal given before and by codein, morphin, or dilaudid, during treatment.

Abdominal cramps, nausea, and vomiting, which accompany treatments by hot air cabinets or diathermy, have been minimized by the use of 500 cc. of a 10 per cent glucose solution given intravenously in a saline medium, as recommended by Desjardins. It is well recognized that tetany is likely to occur in prolonged fever therapy. It is particularly observed in the cabinet method with an unusually high environmental air temperature (140-150 degrees F.). "Hot air to the skin stimulates respiration to such an extent that definite alkalosis is produced." (Stecher.[42]) This condition is easily remedied by the intravenous administration of 10 cc. of calcium gluconate.

We have records of our results of over 350 treatments using electromagnetic induction by sustained fever of 105 degrees F. for a period of five hours. These we consider very favorable: No tetany, no prostrations occurred; no cramps or other evidence of abdominal distress caused discomfort; and only two cases of nausea were observed. One of these vomited. Only two cases of fever blisters were caused by the treatment; one was mild and soon disappeared, while the other necessitated suspension of treatment for a month.

Summary and Conclusion

1. A comparison of malaria therapy with electromagnetic induction has been made. Evidence is at hand that hyperthermy through physical methods is superior to fever produced by foreign proteins. Though the results obtained may be equal to those of the physical methods, the hazards by foreign proteins make physical procedures a method of greater safety. The advantages of the physical methods are:

a. They are always available.

b. The frequency, duration and the high elevation of temperature can be produced in most cases and kept under accurate control.

c. Chemotherapy can be used with pyretotherapy when desired.

d. No pathologic diseases are introduced.

2. Through the use of artificial fever in gonococcal arthritis, 92 per cent of the cases are completely relieved. In bone changes no improvement can be expected other than relief of pain and sterilization of the joint. Fifteen to twenty per cent of atrophic arthritis cases show permanent improvement, though fever treatment should not be used to the exclusion of general treatment. Hypertrophic arthritis evidencing bone changes shows no marked improvement.

3. As the gonococcus is the only microorganism whose lethal rate has been determined, the most favorable results have been obtained in its infections.

4. The value of aseptic, controlled fever therapy as an adjunct to chemotherapy in the management of neurosyphilis is now definitely established.

5. The ability of trained personnel is of great importance in the production of artificial fever.

6. Fever therapy in the treatment of disease is still in the experimental stage, except in neurosyphilis and gonococcic infections, where it has gained recognition as an effective method.

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(For Discussion Turn to Page 289)

Discussion

Dr. J. K. Howles (New Orleans): There is still need for much fundamental, scientific investigation in this branch of therapy, for the "fever-machine business" has become so highly commercialized that often the claims from such sources are distinctly at variance with the scientific facts. This "ballyhoo" has been aided, I am sorry to say, by over enthusiastic members of our profession. It would seem that we are becoming too much concerned with machines, and neglecting the fundamentals behind this therapeutic measure. Fortunately, keen observers like Wagner von Jauregg and his disciples have since proved that the destructive and degenerative process due to the effect of fever was in part imaginary. After years of critical observation of the result of fever in cases of dementia paralytica, von Jauregg, in 1917, proved that artificially induced fever could be used in the treatment of that seemingly hopeless infirmity. It has been a short step from the original evidence of the therapeutic value of fever to the present development of mechanically induced fever. Without endeavoring to extol the value of any particular kind of "fever machine," I have found pyretotherapy, especially that form induced by "fever machines" almost indispensable in the treatment of certain types of central nervous and systemic syphilis. I refer to those syphilitics who do not respond or cannot tolerate the usually effective chemotherapeutic measures.

Although it is generally agreed that the early cases of neurosyphilis offer the best prognosis, we, unfortunately, cannot always select our cases and many far advanced neurosyphilitics are encountered. Even though our hope of cure in these far advanced cases is nil, we still strive to make them more comfortable and to prevent them from becoming public charges by arresting the progress of their disease.

We have treated 33 advanced cases of neurosyphilis with induced fever within the last year. Pyretotherapy has been used as a last resort in those in whom no other form of therapy was of benefit. A careful physical examination and laboratory tests, including blood chemistry and complete blood count was made on each of these patients. The cases chosen for this form of therapy were of syphilitics of the following types: 1. Optic atrophy cases which could not tolerate tryparsemide; 2. C. N. S. cases which showed no response to tryparsemide or Bismarsen therapy; 3. C. N. S. cases which showed no response to malaria therapy followed by chemotherapy. All thirty-three cases were treated with combined fever and specific therapy. Bismarsen and saturated solution of potassium iodide or sodium iodide was given in conjunction with the fever. The intervals between treatments varied from twice weekly to once every two weeks. The number of treatments given and frequency of treatments depended upon the individual tolerance of the patient. Only one fatality resulted and it could not be wholly attributed to the fever therapy.

Our clinical results from electromagnetic induction were more impressive than with an equal number of malaria cases used as a control. Our serological reverse to normal in both the spinal and blood were more rapid than in the malaria cases. We consider fever induced by electromagnetic induction a safer and slightly superior method of hyperpyrexia treatment than that usually produced by malaria.

Dr. John S. Coulter (Chicago): The preceding essayists have critically evaluated the limitations and possibilities of hyperpyrexia by physical agents. It is noted that Dr. Giles states that fever therapy is still in the experimental stage except in neurosyphilis and gonococcic infections. Under the circumstances it is important to stress the contraindications already mentioned. Hyperpyrexia by means of physical agents is only safe when it is given in a hospital after a complete physical and laboratory examination under expert medical and technical supervision. At Northwestern University we did not secure as good results in the treatment of asthma as Dr. Phillips did, hence our Asthma Clinic is not continuing its use. With reference to the use of fever therapy with air conditioned cabinets I should like to ask Dr. Trautman if he has determined if its high temperature has had any effects in sterilizing patients so treated. Experiments at the University of Chicago with high external temperatures have shown a very definite and deleterious effect on the normal function of the testicles.

Dr. Kenneth Phillips (closing): Dr. Coulter emphasized three important points. Fever therapy is a hospital procedure, although there is a surprisingly prevalent opinion that it can be utilized as an office procedure, which, in my opinion is dangerous. I have wondered many times regarding the possibility of sterility resulting from these high temperatures. I think the skin temperature during the fever plays an important rôle in this connection. I wish to reëmphasize that our results in bronchial asthma were not encouraging when fever alone was used. When employed in conjunction with other measures fever is valuable.

Dr. John Trautman (closing): The need for careful management of fever treatments cannot be too strongly emphasized, since deaths have occurred from such treatments. Probably some changes in technic may aid in decreasing accidents. We can only answer Dr. Coulter's question concerning sterilization of patients treated with fever by saying that we have no work to report.

Dr. Upton Giles (closing): Our procedure in producing artificial fever has followed closely the original work of

Neymann and Osborne. While finding their methods effective, we occasionally have resorted to other means of inducing fever. We employed several ways; namely, the conductive, the convective and the conversive methods. One method was an incandescent-light cabinet, the degree of heat being controlled by socket switches. We found that maintaining febrile temperatures of 105 degrees F. for several hours produced symptoms of heat stroke. We therefore soon discontinued the use of cellotex cabinets. Lately, Atsatt and Patterson of the Santa Barbara Cottage Hospital, as well as Bishop, Warren and Lehman, have advocated the incandescent-light method in preference to all others.

The induction of high fever by electromagnetic fields having been developed, we soon followed the lead of others in using a large canvas bag of the zipper type, thus enclosing the patient to prevent heat loss. The use of induced short waves and by means of the cable, pancake-coil, and Kimball Cabinet, afforded us the simplest and safest way of any method used. The pathologic reactions of fever, such as abdominal cramps, nausea, vomiting, tetany, headache, and vasomotor collapse do not occur when this method is used within the range of fever adopted.

Lately there is a tendency to permit the production of artificial fever in homes and in physicians' offices. It is not my purpose to determine the method and the place where artificial fever be induced, but we should realize that, at best, the patient is infrequently brought to the border-line of disaster. It is therefore evident to me that when temperatures of 105 to 106.7 degrees F. are maintained for several hours, there must be constant medical and technical supervision.

Asthmatic cases in our hands have received little benefit from fever therapy.

Regarding the questions propounded by Drs. Phillips and Coulter relative to high environmental temperatures in air-conditioned cabinets producing sterility in the male, we are unable to give any information; but our experiments with animals proved that sterility is produced when the incandescent light cabinet is used. We have set a definite time for the culmination of our observation. Then we will make a final report as to the refuctioning of the generative organs.

Printed in U. S. A.

PRESENT STATUS AND TECHNIC OF ARTIFICIAL FEVER *

UPTON GILES, M.D.

NEW ORLEANS

For the past fifty years physicians[45-50] have suspected that fever might be part of the defensive mechanism of the body against invading microorganisms. It was Wagner-Jauregg,[49] who first successfully produced fever in hopeless paretics by malarial injections, which demonstrated the soundness of the concept. Previous to this time, in the treatment of syphilis, gout, arthritis and other chronic conditions, increased bodily heat was induced mostly by physical measures. These were applications of hot blankets, hot air, hot water, steam and mud from natural or artificial sources. While these measures were used empirically, distinct beneficial results were obtained.

In 1884, Phillips,[52] while visiting Hot Springs, Arkansas, experimented on himself and demonstrated the value of temperature-rising baths. Since Jauregg's epochal experiments, many other methods of producing therapeutic fever have been evolved and used with varying degrees of efficiency and safety.

Of the medical or non-physical methods, the injections of crystalloid and colloid substances[41] and of heteroproteins, such as peptones, milk[54] and casein, may be mentioned. Others have injected vaccines prepared from typhoid, paratyphoid and other microorganisms.[20] Inoculations or organisms from erysipelas, undulant fever,[35] rat bite fever[38] and tertian malaria[12-49] have been employed. These methods, usually classified as physiologic, really should be grouped as pathologic, for they depend upon the reaction of the body to the introduction of a foreign substance. The reaction in different individuals varies, and can neither be predicted nor entirely controlled in all instances.

Effect of Malaria Treatment

Following v. Jauregg's and Kyrle's[23] astounding results in paresis with malarial plasmodia, this form of therapy became widely used both in Europe and America. Although malaria has been our most satisfactory method of treatment in paresis, it has many dangers. In 100 cases reported by Bahr[3] and Breutsch,[4] 23 died during or following the malarial paroxysms. In a recent review of the literature Karnosh and Williams,[26] collated 580 cases of paretics who had received inoculations of malaria. These showed a wide array of symptoms and complications with a death rate of 12.7 per cent. Hemorrhages, hematomas, and non-inflammatory ulcers were considered specific lesions due to malarial infections. Enlargement of the spleen and rupture of this organ in some cases produced shock and immediate death. In addition, after injection of the malarial organism, many rapidly fulminating septic states developed, thus suggesting a symbiotic relationship between the plasmodium and many pathogenic organisms. Evidence of serious complications were noted and include jaundice; cyanosis of varying degrees; paroxysm with a temperature of 105.8 degrees F. lasting eight hours following the chill; blood urea of 60 mg. per 100 cc.; and low temperature accompanying an unusually high pulse and respiratory rate. Regarding re-

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* From the Department of Physical Therapy, Charity Hospital, New Orleans.

* Read at the meeting of the Southern Section, American Congress of Physical Therapy, New Orleans, March 23, 1936.